AMENDMENTS

Specification:

Please replace paragraph [0001] with the amended paragraph below:

[0001] This application claims priority from the provisional patent application Serial No. ~~60/407,677~~ 60/408,677 filed Sep. 7, 2002 in the name of Vincent B. Pizziconi and Timothy Crowley entitled "Self-Energizing, Scalable and Integrative Hybrid Informatic Method and Apparatus to Manipulate, Process, Diagnose and Treat Complex Fluids" incorporated herein by reference.

Please replace paragraph [0031] with the amended paragraph below:

[0031] FIG. 2 is a diagrammatic cross section along the lines [2-2] 28 of FIG. 1 and shows a pair of weir-like filters opening from a main fluid channel to two filtrate receiving side channels;

Please replace paragraph [0035] with the amended paragraph below:

[0035] ~~FIGS. 6A-6C~~ FIGS. 6a-6c are diagrammatic illustrations of a multi-channel analysis chip with electro-optical test provisions;

Please replace paragraph [0042] with the amended paragraph below:

[0042] ~~FIG. 13A~~ FIG. 13a is a top plan view of a silicon-based integrated fluid device incorporating eight filters and a pair of hematocrit meters on a single silicon chip;

Please replace paragraph [0043] with the amended paragraph below:

[0043] ~~FIG. 13B~~ FIG. 13b is an enlarged fragmentary plan view of the device of ~~FIG. 13A~~ FIG. 13a and showing a series of parallel, serpentine capillary flow paths;

Please replace paragraph [0046] with the amended paragraph below:

[0046] ~~FIGS. 16A and B~~ FIGS. 16a and b are plots of hemoglobin concentration and plasma filtrate vs. filter pore width showing, in ~~A~~ (a), individual results, and in ~~B~~ (b), average of three tests per point with filter pores 200 *,urn* long;

Please replace paragraph [0047] with the amended paragraph below:

[0047] ~~FIGS. 17A and B~~ FIGS. 17a and b plots hemoglobin concentration and plasma filtrate vs. filter pore length at three pore heights showing individual results: ~~A~~ (a) an average of three tests per point, and ~~B~~ (b) with filter pores 500 *,urn* wide;

Please replace paragraph [0061] with the amended paragraph below:

[0061] ~~FIGS. 31A and 31B~~ FIGS. 31a and b are plots of expanded channel width vs. viltration channel length first without ~~(A)~~ (a) and then with ~~(B)~~ (b) limitations imposed by wall sheer rate limit and hematocrit design rule limitation.

Please replace paragraph [0076] with the amended paragraph below:

[0076] As shown in FIGS. ~~6A-C~~ 6a-c, a generalized bioanalytical microdevice 100 illustrates the potential impact of microfluidic research on clinical chemistry. This device is a "micro sequential multi-channel analysis chip" (uSMAC) and has the capability to perform, at 16 locations 102, 16 different blood tests from a single drop of blood. This disposable test cartridge 100 contains microfilters, shown diagrammatically in FIG. ~~6B~~

6b at 103 for the separation of plasma, plasma collection chambers 104 for chemical analysis, and optical detection cells 106, FIG. ~~6C~~ 6c, for quantification of the analytes. Analysis is initiated by placing a drop of blood from a finger stick on the inlet reservoir 107. As blood flows through the device via capillary action, plasma is separated by the microfilters located on each of the sixteen analysis channels 109. Each plasma outlet chamber 104 contains analysis reagents FIG. ~~6C~~ 6c and forms a horizontal optical detection cell with a 2 mm long optical path length, requiring only nanoliter volumes of plasma. The test cartridge is evaluated using a handheld device, similar to commercial glucose test systems, containing the optical and electrical systems required to quantify the test results. These may include a laser 110 and a photodetector 112, for example, as shown, viewing the analyte through the glass cover 114 of the device using mirrored sidewalls 111 of the optical detection cell. With large-scale integration of microfluidic and microelectronic devices, it becomes possible to integrate all these functions into a stand-alone test cartridge. As nanotechnology progresses, it is believed it will be possible to develop a fully implantable *,uTAS* system. In any case, the realization of such a device has broad reaching implications for patient care and the availability of sophisticated clinical analysis to the general populace.

Please replace paragraph [0077] with the amended paragraph below:

[0077] Using the design rules and the operation model described herein, a multi-channel microfilter device 115 was designed and fabricated as shown in FIGS. ~~13A and 13B~~ 13a and 13b. This device has the capability to isolate blood plasma in eight separate

microchannels 123 (FIG. ~~13B~~ 13b). The device includes, on a single Si chip 116, eight integrated expanded channel microfilter devices connected to a common input reservoir 118 and utilizing a common air vent line 119. It also uses -8 mm long filtration channels 117 with l0-channel expanded channel sections 121 utilizing a serpentine flow channel layout best illustrated in FIG. ~~13B~~ 13b.

Please replace paragraph [0093] with the amended paragraph below:

[0093] In FIG. ~~7A~~ 7a blood plasma is introduced at a reservoir 131 and travels by capillary action through a flow channel 133 to an output reservoir 135. Along the way the blood plasma passes a series of the weir-style filters 137 of varying lengths. Plasma and any lysed cell is carried by capillary action of tubes 139 to a collection region 141. The tubes 39 and the collection region 141 are vented at 142. FIG. 8 is an enlarged illustration of one of the filters 137 in association with the flow channel 133 and the tube 139 therefrom. Two pores 143 and 144 are shown. Each has a length I and a width w.

Please replace paragraph [0094] with the amended paragraph below:

[0094] Similarly, FIG. ~~7B~~ 7b illustrates a hemolysis test device of variable filter width w. It has an input reservoir 151 from which blood flows along a flow path 153 to an outlet reservoir 155. Filters 157 have varying pore widths w. The core width w is illustrated in FIG. 8. Again tubes 159 carry plasma by capillary action to a collection region 161 vented to atmosphere at 162.

Please replace paragraph [0098] with the amended paragraph below:

[0098] Hemolysis testing and evaluation was performed on 115 individual microfilter test structures. The volume of plasma and the concentration of hemoglobin in the plasma was quantified for each device and compared to filter parameters of pore height, width, and length. Test devices were fabricated on three silicon wafers, each wafer included five filter length and five filter width test devices (FIGS. ~~7A-7B~~ 7a-7b). Each wafer was fabricated at one of three pore heights, 0.37, 0.67, or 1.28 urn. The average channel height of the blood flow and plasma outlet channels was 21 urn.

Please replace paragraph [0167] with the amended paragraph below:

[0167] When the operational model is applied over a wide range of device dimensions, a portion of the evaluated design space typically will not satisfy the design rule requirements for the minimum expanded channel wall shear rate or maximum change in hematocrit or both. If these constraints are not met, the operation model assigns a zero value for the plasma volume isolated. For example, the upper right orner of FIG. 30 shows the portions of the design space that did not meet the minimum shear rate requirement, and this area was assigned a zero plasma volume value. In a second example of operational modeling (FIGS. ~~31A&B~~ 31a & b), the effect of both the hematocrit and minimum wall shear rate design rules on the usable design space can be seen. The top panel of FIGS. ~~31A&B~~ 31a & b shows an operational model that is unconstrained by the hematocrit design rule, and the bottom panels shows the reduction in available design space when the hematocrit design rule is applied. The hematocrit design rule significantly reduces the usable design space, and prohibits the

attainment of the optimal design condition. Recall that the hematocrit design rule was implemented to avoid a large increase in apparent expanded channel viscosity and associated blood instability. In part this constraint is due to the formation of a blood cell plug at the leading edge of the flow, and this example, once again, illustrates how this phenomenon negatively impacts device design and optimization.

Please delete paragraphs [0169]-[0179].